Engineering a Cardiovascular Tissue Graft from Human Embryonic Stem Cells

Grant Award Details

Engineering a Cardiovascular Tissue Graft from Human Embryonic Stem Cells

Grant Type: Comprehensive Grant

Grant Number: RC1-00151

Investigator:

Name:	Christopher Zarins
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,454,490

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Engineering a Cardiovascular Tissue Graft from Human Embryonic Stem Cells

Public Abstract:

Cardiovascular disease (CVD) affects more than 71 million Americans and 1.7 million Californians. Recently, engineered cardiovascular tissue grafts, or “patches”, including one made from mouse embryonic stem cells (ESC), have shown promising results as a future therapy for CVD. Our overall goal is to extend these recent results to human ESC as follows.

Aim 1: Apply mechanical stretch and electrical pacemaker-like stimulation to hESC-derived heart cells in order to make them stronger and beat at the same time. Current methods to turn hESC into heart cells do not result in the organization required to generate enough strength to support a weak heart and to avoid irregular heart beats. We will use specially engineered devices to apply mechanical stretch and electrical pacemaker-like stimulation to hESC-derived heart cells in order to strengthen them and make them beat in unison.

Aim 2: Engineer a cardiovascular patch from hESC-derived heart cells in order to make a potential new therapy for heart disease. Recently, heart cells from mouse ESC, supporting structures called scaffolds, and mechanical stretch have successfully been combined to engineer a cardiovascular patch. We will combine the hESC-derived heart cells from Aim 1, scaffolds, and the same stretch and pacemaker-like stimulation as in Aim 1 to engineer a cardiovascular patch. In addition, we will add a specialized substance called VEGF to our patch so that, potentially, a blood supply will form around it after it is implanted on a diseased heart. We believe a blood supply will be necessary to keep our patch healthy, and in turn, this will allow our patch to help a damaged heart pump better.

Aim 3: Assess whether our patch can remain healthy and also strengthen the heart of a rat after it has undergone a heart attack. We will first implant our cardiovascular patch in the rat aorta, the main blood vessel that supplies blood to the body, to test whether the patch remains healthy and whether it can contract and beat on its own. We will first use the aortic position because we feel it will allow us to assess the inherent function of the patch, thus facilitating our efforts to improve its design. After testing in the aortic position, we will implant the patch over damaged heart tissue in a rat that has undergone an experimentally created heart attack. Over a period of several weeks, we will use novel imaging techniques, ultrasonography, echocardiography, and electrocardiography to non-invasively test whether the patch remains healthy and whether the patch helps the damaged heart pump better.

We believe the above aims will address questions relevant to hESC-based cardiovascular therapies and will provide vital information needed for safe and effective future clinical translation. As we will evaluate both federally and non-federally approved cell lines, and thus unlikely to receive federal funding, we will need to rely on the support provided by CIRM to carry out our objectives.

Statement of Benefit to California:

Cardiovascular disease (CVD) affects more than 1.7 million Californians and 71 million Americans. The societal and financial impacts are tremendous, with CVD accounting annually for an estimated $8 billion in CA and nearly $400 billion in US health care costs.

In the case of chronic illness such as CVD, the state and national health care systems may not be able to meet the needs of patients or control spiraling costs, unless the focus of therapy switches away from maintenance and toward cures. Fortunately, the passage of Proposition 71 in 2004, and the subsequent creation of the California Institute for Regenerative Medicine (CIRM), has created the funding needed to advance human embryonic stem cell (hESC) research that could lead to curative therapies that would benefit both millions of Californians and Americans.

Recently, engineered cardiovascular tissue grafts, made from rat neonatal cardiomyocytes (CM) and cardiomyocytes derived from mouse ESC, have shown promising results as a future therapy for CVD. The overall goal of our proposed research is to extend these recent studies to hESC and engineer a hESC-CM based cardiovascular tissue graft as a regenerative therapy for CVD.

We believe the objectives of our research will benefit the people and the state of California by addressing questions relevant to hESC-based cardiovascular regenerative therapies and will provide vital information needed for safe and efficacious future clinical translation.

Development of cures for diseases such as CVD could potentially improve the California health care system by reducing the long-term health care cost burden on California. In addition, the results of our research may provide an opportunity for California to benefit from royalties, patents, and licensing fees and benefit the California economy by creating projects, jobs, and therapies that will generate millions of dollars in new tax revenues in our state. Finally, stem cell research such as ours could further advance the biotech industry in California, serving as an engine for California's economic future.

We have assembled a multidisciplinary team of experienced investigators to attack the objectives of our proposed research. At the same time, we will train and mentor a new generation of bright students and junior scientists in the areas of hESC biology, regenerative medicine, and technology development. This ensures that an essential knowledge base will be preserved and passed on to both investigators and patients within and beyond California.

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